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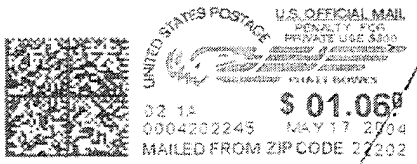


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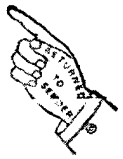

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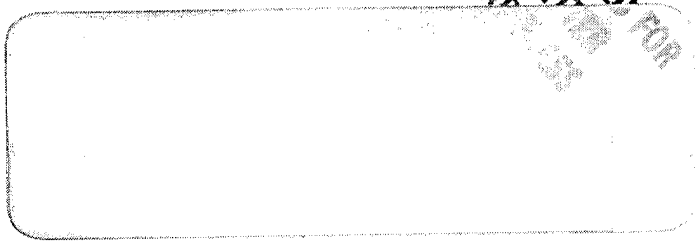

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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/625,221 | 07/22/2003 | Patrick M. Schlievert | 600.311USD1 | 8132 |

7590 05/17/2004

Attention of Mark T. Skoog
MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903

| EXAMINER | |
|---|---|
| GRASER, JENNIFER E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/625,221 | SCHLIEVERT ET AL. | |
| | Examiner | Art Unit | |
| | Jennifer E. Graser | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *40-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/22/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Priority*

1. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a Divisional of Application No. 08,973,391, now U.S. Patent No. X, filed 3/12/98, which is a CIP of....." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

### *Specification*

2. The disclosure is objected to because of the following informalities:

In the "Brief Description of the Drawings", "Figure 4", "Figure 5", and "Figure 6" must be changed to "Figure 4A and 4B", "Figure 5A and 5B", and Figure "6A and 6B" so that they properly correspond to the Drawings.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 40-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40-44, 50, 52, and 54 are vague and indefinite because the claim fails to teach what the substitution of the amino acid should be substituted with, thereby leaving

it unclear as the structure of the claimed nucleic acid. Instead, the claims broadly allow for the change to the nucleic acid to encode any amino acid whether it is positively(negatively) charged amino acid, an uncharged amino acid or a hydrophobic(hydrophilic) amino acid. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The specific substitution, i.e., asparatine-20 to aspartic acid.

Claims 56, 59 and 60 are vague and confusing due to the phrases "a polynucleotide having the portion of sequence SEQ ID NO: 12 that encodes a polypeptide having the sequence of SEQ ID NO:14" and "a polynucleotide having 99% sequence identity with the portion of sequence SEQ ID NO: 12 that encodes a polypeptide having the sequence of SEQ ID NO:14". The claims should be amended so that the phrase "portion of sequence SEQ ID NO: 12 that encodes a polypeptide having the sequence of SEQ ID NO:14" positively recites the portion by sequence position number, i.e., a polynucleotide consisting of nucleotides A-D of SEQ ID NO:12 (wherein A-D are the specific nucleotides which encode SEQ ID NO:14). This wording would clarify the claim.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 40-44, 50, 52, and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

These claims are not enabled because they do not specify the specific amino acid to which the designated SPE-A amino acid is to be changed to. Instead, the claims broadly allow for the isolated nucleic acid molecules to encode any whether it is a positively(negatively) charged amino acid, an uncharged amino acid or a hydrophobic(hydrophilic) amino acid. The specification teaches that the nucleic acid molecules encode polypeptides to be used in compositions, vaccines and methods of providing protection against wild type SPE-A toxin comprising this breadth given the unpredictability set forth in the Examples provided in the instant specification and the examples taught in the prior art.

The specification and prior art both teach that the results from the substitution of amino acids in the SPE-A mutant is very unpredictable. To change a charged amino acid to an uncharged amino acid changes the chemical nature of the compound which has been shown to negatively impact its function. The specification has shown that substitutions of amino acids, even with the same charge, can cause the resultant SPE-A to lose immunogenicity and it's ability to provide immune protection. Due to the highly unpredictable nature of determining acceptable substitutions, it has been necessary to

provide specific results and direction as to what the changes may be. Applicants provided these results in the Declaration of Dr. Patrick M. Shlievert submitted in parent case 08/973,391. However, claims which allow for open-ended changes, i.e., that do not recite what the specific substitution can be, are not enabled. There is no showing in the instant specification of the consequences of these broad mutations or their ability to produce a polypeptide which would provide an immune effect in a host. Both the prior art and specification have shown that even when an amino acid of SPE-A toxin is replaced with an amino acid of the same charged, i.e., conservative substitution, it does not guarantee that the SPE-A toxin will retain it's function. The prior art and specification have shown in several instances that such substitutions have resulted in a toxin with reduced immune function. There is also no evidence provided in the specification which indicates whether or not the specific mutants actually have the various claimed properties, i.e., nonlethality, decrease in mitogenicity, not enhancing endotoxin shock , etc.. The number of mutant SPE-A toxins to be encoded by the claimed nucleic acids encompassed by the instant claims is vast and would not allow one of skill in the art a reasonable expectation of success that any mutant encompassed by the instant claims would have the claimed properties. Specific guidance is needed for the skilled artisan to make a reasoned decision of which mutants would likely have the most success in producing polypeptides which would be effective in vaccine compositions. It is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino

acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spatial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. To start with the DNA sequence first, this requires even more work on the part of the skilled artisan. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different amino acid substitutions and the nature and extent of the changes that can be made.

Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions and their effect on the immunogenicity of the SPE-A toxin they encode, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

***Allowable Subject Matter***

7. Claims 45-49, 51, 53, 55, and 56-60 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second and first paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

8. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571)

272-0858. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

5/13/04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|---|---|---|---|
| Applicant: | SCHLIEVERT ET AL. | Examiner: | UNKNOWN |
| Serial No.: | 10/625,221 | Group Art Unit: | 1645 |
| Filed: | JULY 22, 2003 | Docket No.: | 600.311USD1 |
| Confirmation No.: | UNKNOWN | Customer No.: | 23552 |
| Title: | MUTANTS OF STREPTOCOCCAL TOXIN A AND METHOD OF USE | | |

CERTIFICATE UNDER 37 CFR 1.8:
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, with sufficient postage, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on October 22, 2003.

By: Sheryl A. Boerboom
Name: Sheryl A. Boerboom

**INFORMATION DISCLOSURE STATEMENT (37 C.F.R. § 1.97(b))**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner.

This statement should be considered because it is submitted within three months of the filing date of the above-identified application, which is not an application under 37 C.F.R. § 1.53(d). Accordingly, no fee is due for consideration of the items listed on the enclosed Form 1449.

In accordance with 37 C.F.R. §1.98(d), a copy of each document or other information listed on the enclosed Form 1449 is not provided because it was previously cited by or submitted to the U.S. Patent and Trademark Office in parent application, U.S. Serial No. 08/973,391 filed on March 12, 1998.

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that a

reference has been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Pursuant to the provisions of M.P.E.P. 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2725.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903
(612) 332-5300

DATE: Oct 22, 2003

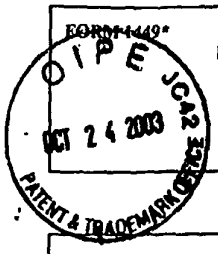
Mark T. Skoog

Mark T. Skoog
Reg. No. 40,178

23552
PATENT TRADEMARK OFFICE

Date Mailed: October 22, 2003






| FORM 1449* | INFORMATION DISCLOSURE STATEMENT | Docket Number: 600.311USD1 | Application Number: 10/625,221 |
|---|---|---|---|
| | IN AN APPLICATION | Applicant: SCHLIEVERT ET AL. | |
| | (Use several sheets if necessary) | Filing Date: July 22, 2003 | Group Art Unit: 1645 |

**U.S. PATENT DOCUMENTS**

| EXAMINER INITIAL | DOCUMENT NO. | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|---|---|---|---|---|---|---|
| | 5,336,598 | 08/09/1994 | Kotzin et al. | | | |
| | 5,298,396 | 03/29/1994 | Kotzin et al. | | | |
| | | | | | | |

**FOREIGN PATENT DOCUMENTS**

| | DOCUMENT NO. | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION | |
|---|---|---|---|---|---|---|---|
| | | | | | | YES | NO |
| | WO 93/14634 | 08/05/1993 | PCT | | | | |
| | WO. A, 85 00832 | 02/28/1985 | PCT | | | | |
| | | | | | | | |

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

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| EXAMINER | | DATE CONSIDERED | 9/13/04 |
|---|---|---|---|

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

*Substitute Disclosure Statement Form (PTO-1449)

| FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary) | Docket Number: 600.311USD1 | Application Number: 10/625,221 |
|---|---|---|
| | Applicant: SCHLIEVERT ET AL. | |
| | Filing Date: July 22, 2003 | Group Art Unit: 1645 |



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| EXAMINER | DATE CONSIDERED 5/23/04 |
|---|---|

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

| FORM 1449* INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION (Use several sheets if necessary) | Docket Number: 600.311USD1 | Application Number: 10/625,221 |
|---|---|---|
| | Applicant: SCHLIEVERT ET AL. | |
| | Filing Date: July 22, 2003 | Group Art Unit: 1645 |



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| EXAMINER | DATE CONSIDERED 5/13/04 |
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.